REMARKS

Applicants express gratitude to the Examiner for the interview held on November 10, 2011.

In view of the foregoing amendments, reconsideration and withdrawal of the outstanding Office Action rejections is respectfully requested. Claims 237-294 have been cancelled and claims 295-324 have been added. No new matter has been added.

The priority application, U.S. 60/094,690, provides written description support for the present claims, *inter alia*, as follows:

Support for tissue repair and regeneration is found, *inter alia*, on page 3, lines 19-21, the paragraph bridging pages 6 and 7, and page 7 (as a whole).

Support for targeting specific cells of tissue to be treated is found, *inter alia*, in the paragraph bridging pages 9 and 10.

Support for systemic administration is found, *inter alia*, on page 3, lines 23-25, page 4, lines 11-14 and lines 18-21, page 9, line 14, and Example 1 on page 23.

Support for topical administration is found, *inter alia*, on page 4, lines 11-17 and lines 21-23, page 9, line 14, and Example 1 on page 23.

Support for administering Tβ4 with a pharmaceutically acceptable carrier is found, *inter alia*, on page 16, lines 21-23.

Support for accelerating repair of tissue compared to untreated tissue is found, inter alia, in the paragraph bridging pages 9 and 10, the Examples, and Figures 2 and 3.

Interview Summary

The Office Action of 8/3/11 was discussed. The 112 reiection was discussed. The examiner noted that page 18 of the specification provides direction for certain terminology. It was noted that certain references teach thymosin fraction 5. The examiner noted that such fraction is a purified fraction which has been purified from other components. Alternate claim language to exclude prior art teachings of thymosin fraction 5 were discussed, however no final agreement was reached. The 102 rejection based on Turischev was discussed. It was noted that Turischev teaches administration to rats and if the claims required a patient population other than rats that Turischev would not be applicable under 102, although it may be applicable under 103. The Goldstein reference as used in the previous 102 rejection was discussed. The examiner noted that example 5 (column 9) teach incisions thus the broad limitation of 'in need of tissue repair' is met. The examiner noted that applicants could consider trying to more specifically identify the patient population of the instant claims. With respect to 103 rejections, the examiner noted that applicants can provide any evidence that they have of unexpected results. The examiner noted that even if the claims are amended to overcome the current 102 rejections, that numerous references may be applicable for 103 rejections.

Response to Objections to Specification

The specification was objected to for lacking reference to sequence identifiers on page 10 and in Figures 10 and 11. Applicants submit that page 10 has been amended to insert sequence identifiers. Applicants note that page 10 was amended to insert a sequence identifier in the amendment filed on January 3, 2002, however the remaining pages of the amendment were mistakenly not filed. Page 10 of the specification was also amended in the amendment filed on August 31, 2009. Therefore, the present amendments to page 10 insert sequence identifiers where they were previously not inserted.

The Examiner also states that Figures 10 and 11 lack sequence identifiers. Applicants respectfully submit that according to MPEP § 2422.02, when a sequence is presented in a drawing, the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings. Applicants submit that in the amendments to the specification filed on January 3, 2002, the Brief Description of Figure 10 was amended to reflect that the sequence shown was SEQ ID NO:2. Therefore, Applicants submit that this requirement has already been met.

A replacement Figure 11a is being submitted that includes sequence identifiers.

Accordingly, Applicants respectfully request that the objections be withdrawn.

Response to Rejections under 35 U.S.C. § 112

Claims 265 and 292 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Patent Office asserts that the term "substantially free" is unclear. Without acceding to the proprieties of the assertion made in the Office Action, Applicants submit that this rejection has been rendered moot by the deletion of claims 265 and 292.

Claims 260-264, 267-272, 275- 276, 278, 281, 282, 287-289, and 291-294 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Patent Office asserts that there is a lack of literal support for the listed claims when given the broadest possible interpretation. Without acceding to the proprieties of the assertion made in the Office Action, Applicants submit that this rejection has been rendered moot by the deletion of claims 260-264, 267-272, 275-276, 278, 281, 282, 287-289, and 291-294.

Response to Rejections under 35 U.S.C. § 102

Claims 237, 240-242, 244, 247, 248, 253-256, 259-272, 275, 276, 278, 281, 282, 287-289, and 292-294 were rejected under 35 U.S.C. § 102(b) as being anticipated by Turischev as evidenced by Mann.

In the Office Action, it is asserted that Turischev discloses that 'thymosin' is effective in healing flat skin wounds in rats. The Office Action asserts that Turischev disclose results of experiments involving removing a skin flap from the backs of rats and administering Thymosin Fraction 5 (TF5) to the rats, either intraperitoneally or topically. The Office Action asserts that Turischev discloses that there is clear acceleration of the healing rates and that a dose of 0.8 µg accelerated wound healing.

The Office Action acknowledges that Turischev does not recite the components of thymosin 5 fraction, but asserts that Mann discloses (column 4 lines 8-53) that thymosin fraction 5 contains thymosin beta 4 (column 4 line 31) and thymosin alpha 1 (column 4 line 26). Accordingly, the Office Action asserts that Turischev discloses administering a composition containing thymosin beta 4 either topically or intraperitoneally.

Insofar as this rejection could apply to the present claims, it is respectfully traversed.

The previously pending claims have been cancelled and replaced with claims 295-324. The newly presented claims are not anticipated by, or even remotely rendered obvious by Turischev as evidenced by Mann.

Independent claim 295 recites "[i]n a method for treating tissue in a human with

thymosin beta 4 (Tβ4), the method comprising targeting cells of said tissue to be treated prior to administration of said Tβ4, then administering said Tβ4 to said targeted tissue so as to promote repair and revitalization of said tissue, wherein said Tβ4 is administered in an amount effective to promote repair and revitalize said tissue." Applicants submit that Turischev does not anticipate the subject matter of independent claim 295 at least because it does not disclose a method of treating a human, a method of treating a human with Tβ4, targeting cells of said tissue to be treated prior to administration of Tβ4, administering Tβ4 to the targeted tissue so as to promote repair and revitalization of the tissue, or administering Tβ4 in an amount effective to promote repair and revitalize the tissue. Accordingly, Applicants respectfully request that the rejection be withdrawn. Further, the dependent claims should be free of Turischev for the same reasons as the base claim and further due to the additional features that they recite.

Claims 267, 268, 270, 275, 278, 282, 287-289, and 292-294 were rejected under 35 U.S.C. § 102(b) as being anticipated by Goldstein (U.S. 5,578,570) as evidenced by Lai (U.S. 5,358,703). The Patent Office asserts that Goldstein discloses treating septic shock by administering thymosin beta 4 to humans in a dose of 0.4-4 mg/kg intravenously. The Examiner asserts that Lai evidences that those with septic shock are in need of tissue repair. Applicants respectfully disagree and traverse the rejection.

Insofar as this rejection could apply to the present claims, it is respectfully traversed.

The previously pending claims have been cancelled and replaced with claims 295-324. The newly presented claims are not anticipated by, or even remotely rendered obvious by Goldstein as evidenced by Lai.

Independent claim 295 recites "[i]n a method for treating tissue in a human with thymosin beta 4 (Tβ4), the method comprising targeting cells of said tissue to be treated prior to administration of said Tβ4, then administering said Tβ4 to said targeted tissue so as to promote repair and revitalization of said tissue, wherein said Tβ4 is administered in an amount effective to promote repair and revitalize said tissue." Applicants submit that Goldstein does not anticipate the subject matter of independent claim 295 at least because it does not disclose a method of targeting cells of tissue to be treated prior to administration of Tβ4, administering Tβ4 to the targeted tissue so as to promote repair and revitalization of the tissue, or administering Tβ4 in an amount effective to promote repair and revitalize the tissue. Accordingly, Applicants respectfully request that the rejection be withdrawn. Further, the dependent claims should be free

of Goldstein for the same reasons as the base claim and further due to the additional features that they recite.

Response to Rejections under 35 U.S.C. § 103

Claims 237, 240-242, 244, 247, 248, 253-256, 258-272, 275, 276, 278, 281, 282, 287-289, and 291-294 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Goldstein and Lai and Palladino (U.S. 5,055,447). Insofar as this rejection could apply to the present claims, it is respectfully traversed.

The Patent Office acknowledges that Goldstein does not reduce to practice using topical administrations and does not disclose use of transforming growth factor beta. However, the Patent Office asserts that Palladino discloses treating septic shock by administering transforming growth factor beta.

Applicants submit that the rejected claims have been cancelled and replaced with the above new claims. For the reasons outlined above, Applicants have shown that independent claim 295 is not anticipated by Goldstein, as evidenced by Lai. Palladino does not remedy the deficiencies of Goldstein because Palladino is only related to administering TGF-beta. Accordingly, claims depending from independent claim 295 are distinguished for at least the above reasons.

Independent claim 295 recites "[i]n a method for treating tissue in a human with thymosin beta 4 (Tβ4), the method comprising targeting cells of said tissue to be treated prior to administration of said Tβ4, then administering said Tβ4 to said targeted tissue so as to promote repair and revitalization of said tissue, wherein said Tβ4 is administered in an amount effective to promote repair and revitalize said tissue." Applicants submit that Goldstein does not suggest the subject matter of independent claim 295 at least because it does not relate to a method of targeting cells of tissue to

be treated prior to administration of Tβ4, administering Tβ4 to the targeted tissue so as to promote repair and revitalization of the tissue, or administering Tβ4 in an amount effective to promote repair and revitalize the tissue. Neither Palladino nor Lai remedy the deficiencies of Goldstein. Accordingly, Applicants respectfully request that the rejection be withdrawn. Further, the dependent claims should be free of Goldstein, Lai, and Palladino for the same reasons as the base claim and further due to the additional features that they recite.

Applicants also note that Goldstein is drawn to obstructing progression of a sepsis cascade in a mammal. In all of the Goldstein examples, Tβ4 must be administered simultaneously or within 5 minutes of administration of the endotoxin in order to have a protective effect. Moreover, Goldstein's examples demonstrate that Tβ4 must also be administered two more times after the initial dose in order for the mice to survive. *See* Table I. It is well-known that tissue damage resulting from septic shock does not manifest until the late stages of septic shock, typically when the subject is near death. At the stage that Goldstein administers Tβ4, i.e., simultaneously with injection of the endotoxin or immediately thereafter, there would have been no reasonable expectation that the subjects had already progressed to septic shock. Goldstein aims to block progression of the sepsis cascade so that septic shock does not occur. *See* col. 2, lines 31-48. There is no indication in Goldstein that the sepsis cascade has progressed to the stage where tissue damage sets in and that Tβ4 treats the tissue damage at this stage. Moreover, there is no suggestion in Goldstein that tissue damage has occurred and can be treated by administering Tβ4. Indeed, neither

Goldstein nor Lai provide such evidence or suggestions. Moreover, Lai discloses that septic shock is "manifested by hypotension, a reduced response to vasoconstrictors...and multi-organ failure." (Lai, col. 1:41-45.) If one were to accept the logical reasoning applied in the Office Action on its face, Goldstein can also be said to anticipate or render obvious methods of treating one or more of hypotension, a reduced response to vasoconstrictors, and multi-organ failure in any animal using Tβ4 because Lai discloses that septic shock is manifested by these conditions as well. It is clear that such logic fails because for a reference to anticipate a claim under 35 U.S.C. § 102, the Patent Office has a burden to prove that the reference has an "enabled disclosure" and/or that a characteristic not disclosed in the reference is inherent. M.P.E.P. § 2131.01. Moreover, as the Supreme Court has stated, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006)). The knowledgeable person of skill in the art must have had both a reason to combine the elements "in the fashion claimed" and a predictability of the result. *See KSR*, 550 U.S. at 417-418; *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007) ("[T]he burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so.").

For the same reasons that the above logic, if it was directed against claims

drawn to methods of treating hypotension, a reduced response to vasoconstrictors, or multi-organ failure, fails to satisfy the tests under 35 U.S.C. §§ 102 and 103, and such an application of Goldstein would not be upheld, the present rejections based on Goldstein are also improper. Here, the Patent Office has failed to carry its burden of demonstrating that 1) Goldstein provides an enabling disclosure for treating tissue in a human, 2) tissue damage is an inherent condition that was treated by Goldstein, or 3) a person of ordinary skill would have had reason to attempt to carry out the claimed process, and would have had a reasonable expectation of success. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Response to Provisional Double Patenting Rejections

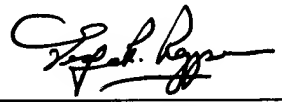
Various combinations of previously pending claims remained provisionally rejected under the doctrine of non-statutory double patenting over separate co-pending patent applications. Applicants continue to request that all provisional rejections on grounds of double patenting be held in abeyance until such claims have been indicated to be allowable and it becomes possible to determine whether claims directed to the same invention or an obvious variant thereof would be issued in more than one patent.

Conclusions

In light of the foregoing, Applicants submit that all outstanding rejections have been overcome. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all the outstanding rejections. Early and favorable action is awaited.

The Commissioner is hereby authorized to charge any fees and to credit any overpayments that may be required with respect to this paper to Counsel's Deposit Account No.02-2135.

Respectfully submitted,

By: 

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